

## **Epidemiology of inflammatory bowel diseases in the elderly in the province of Liège : A three-year prospective study**

### **Epidémiologie des maladies inflammatoires du tube digestif chez le sujet âgé: étude prospective de trois ans**

Patricia PIRONT, Edouard LOUIS, Pascale LATOUR, Olivier PLOMTEUX, Jacques BELAICHE

*Service de Gastroentérologie, CHU of Liège, Belgique.*

#### **SUMMARY**

**Objective** — Inflammatory bowel diseases (IBD) are heterogeneous diseases which affect preferentially young adults. The late onset could represent a particular form of expression of these diseases. The aim of our prospective study was to describe the incidence of IBD in patients older than 60 years as well as their clinical pattern in comparison with a population younger than 60.

**Methods** — A standardized questionnaire for each new case diagnosed in the province of Liège between 01/06/1993 and 31/05/1996 was completed.

**Results** — During the three years, 270 patients were enrolled. In group IBD > 60 years old, there were 60 new cases, including 23 cases with Crohn's disease (CD) (38%), 30 with ulcerative colitis (UC) (50%), and 7 with undetermined colitis (IC) (12%). The proportion of CD was significantly lower in the group IBD > 60 years old than in the group < 60 (114 CD (54%), 81 UC (39%) and 15 IC (7%);  $P = 0.04$ ). The annual incidence tended to be higher for UC than for CD in group IBD > 60 (4.5 and 3.5 per 100,000, respectively) while it was the contrary in younger patients (3.4 and 4.8 per 100,000, respectively). There was no striking difference in the clinical features for both diseases in the two groups, except more frequent diarrhea, weight loss and extraintestinal symptoms in CD patients < 60 years old.

**Conclusions** — In the province of Liège, the incidence of IBD in people older than 60 years is high. IBD in the elderly is characterized by a lower proportion of CD than in the younger population. Clinical features tend to be the same whatever the age at diagnosis for each disease.

#### **RÉSUMÉ**

**Objectif** — Les maladies inflammatoires du tube digestif sont des affections hétérogènes qui touchent préférentiellement l'adulte jeune. Les maladies à révélation tardive pourraient représenter une forme particulière de ces affections. Cette étude prospective a pour but d'étudier l'incidence et le profil clinique de ces maladies chez les sujets âgés de plus de 60 ans.

**Méthodes** — Chaque nouveau cas identifié dans la province de Liège entre le 01.06.1993 et le 31.05.1996 a été enregistré et un questionnaire spécifique a été rempli.

**Résultats** — Durant ces trois années, 270 malades ont été recensés. Soixante étaient âgés de plus de 60 ans, comprenant 23 cas de maladie de Crohn (MC) (38 %), 30 de rectocolite hémorragique (RCH) (50 %) et 7 de colite indéterminée (CI) (12 %). La proportion de MC était statistiquement plus faible chez les sujets de plus de 60 ans que chez les sujets de moins de 60 ans (114 MC (54 %), 81 RCH (39 %) et 15 CI (7 %);  $P = 0,04$ ). L'incidence annuelle de la RCH avait tendance à être plus élevée que celle de la MC dans le groupe de plus de 60 ans (4,5 et 3,5/100000, respectivement) alors que c'était le contraire en dessous de 60 ans (3,4 et 4,8/100000, respectivement). Les caractéristiques cliniques ne différaient entre les deux groupes d'âge que pour la fréquence de la diarrhée, de la perte de poids et des manifestations extra-intestinales, plus importante dans la MC chez les malades < 60 ans.

**Conclusions** — Dans la province de Liège, l'incidence des maladies inflammatoires du tube digestif chez le sujet

âgé de plus de 60 ans est relativement importante, la proportion de maladie de Crohn étant plus faible que chez le sujet jeune. Les caractéristiques cliniques de ces maladies au diagnostic tendent à être semblables quel que soit l'âge du malade.

Inflammatory bowel diseases (IBD) including Crohn's disease (CD) and ulcerative colitis (UC) are multifactorial diseases with both environmental and genetic influences. Recent epidemiological and molecular data suggest some heterogeneity among both CD and UC [1-6]. The identification of subgroups of IBD patients would represent a consistent progress in the understanding and probably the management of these patients. However, the definition of stable phenotypes remains a difficult task since clinical characteristics such as location or behavior of the disease may change over time [7]. In opposition, age at onset is easy to define and remains stable over time. The onset of IBD is usually observed during the second and the third decade of life. A second incidence peak has been described between the age 60 and 80 [8-15]. However, different studies have shown controversial data on this point with no second peak clearly defined [16, 17] or a peak for only UC [18, 19] or CD [20]. The late onset of IBD could represent a different form of expression of these diseases.

In the present work, we used the data of a previously published prospective study on incidence of IBD in the province of Liège [9]. Our aim was to specifically assess the incidence of IBD in the elderly in our area and to compare the clinical features of older patients with IBD with those of younger ones diagnosed during the same period of time.

### **Patients and methods Population**

This prospective study was conducted between the 1<sup>st</sup> of June 1993 and the 31<sup>st</sup> of May 1996. The population was similar to that of our three-year prospective study [9]. Briefly, the province of Liège included 1,014,684 inhabitants (1994 national population census) of whom 222,126 were more than 60 years old.

Diagnosis of CD and UC was assessed by the clinical, morphological and histological criteria of Gower-Rousseau et al. [16]. Patients with a case history of chronic colitis compatible with both the diagnosis of CD or UC were defined as undetermined colitis (IC). The diagnosis was assessed again 6 months later. The following data were collected from a standardized questionnaire filled out by the gastroenterologists of the Société Liégeoise de Gastroentérologie: age, sex, diagnosis delay, disease location, clinical features and family history of IBD.

### **Incidence calculation**

The incidence rates were calculated by dividing the mean numbers of new cases over the three years by the number of inhabitants older or younger than 60 years respectively.

### **Statistics**

Groups and subgroups of patients were compared using t test and chi-squared test. Differences were considered significant when the P value was < 0.05. Logistic regression and stepwise multivariate analysis incorporating all the compared parameters were also performed.

### **Results Incidence**

During the three years, 270 newly diagnosed cases of IBD were recorded. Sixty patients were more than 60 years old (22%) (IBD > 60) and 210 patients were less than 60 years old (78%) (IBD < 60). The incidence of IBD in patients older than 60 years was 9/100.000 inhabitants/year and that of patients younger than 60 years was 8.8/100.000.

The distribution of CD, UC and IC in the two groups is shown in figure 1. There was a significantly lower proportion of CD in group IBD > 60 than in group IBD < 60, 38 and 54% respectively (P = 0.04) (table I). The proportion of IC was not statistically different in the two groups, 12 and 7% respectively.

The incidence rate was slightly higher for UC than for CD in group IBD > 60 (4.5 and 3.45 per 100,000 respectively), while it was slightly higher for CD than UC in group IBD < 60 (4.8 and 3.4 per 100,000 respectively). These differences did not reach statistical significance. There were two peaks of age-specific incidence for UC and CD (figure 2): the mean age at the time of diagnosis in group IBD > 60 was 66.8 years (60-84) for CD and 68.6 years (61-80) for UC. In group IBD < 60, it was 30.3 years (15-54) for CD and 34.3 years (13-59) for UC.

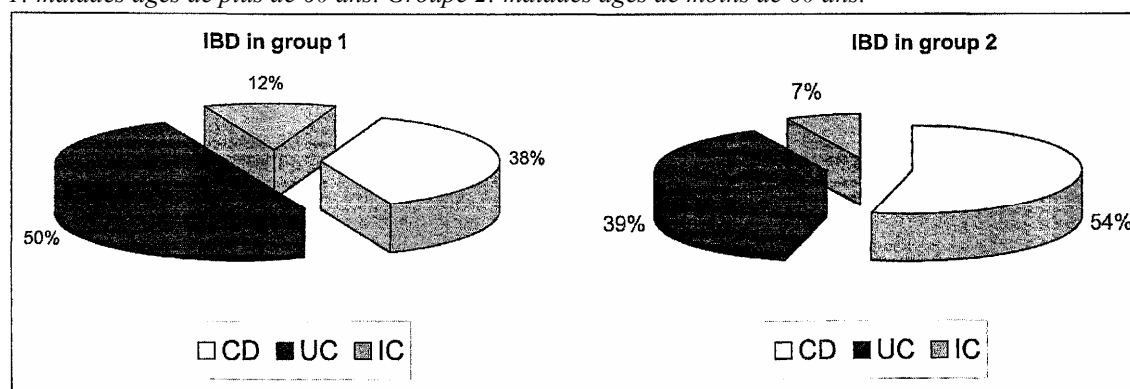
### Demographic data

Tables I and II show the main characteristics of the diseases. The intervals between the onset of symptoms and the diagnosis as well as the pattern of disease were not different between CD and UC patients.

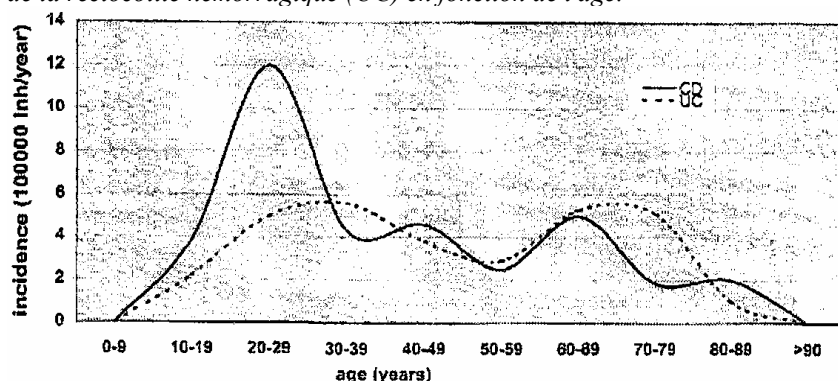
### Clinical manifestations

Tables III and IV show the main clinical characteristics of the diseases in the two groups of patients. The only statistically significant difference concerns Crohn's disease: diarrhea, weight loss and extraintestinal symptoms were more frequent among patients younger than 60 at diagnosis than in patients older than 60. The multivariate analysis showed no further difference between the two groups in patients with UC. In patients with Crohn's disease, it did not select the three clinical characteristics which were statistically significant in univariate analysis.

**Fig. 1** - Repartition of cases of Crohn's disease (CD), ulcerative colitis (UC) and indetermined colitis (IC) in the two groups. Group 1 = patients > 60 years old. Group 2 = patients < 60 years old. Répartition des cas de maladie de Crohn (CD), rectocolite hémorragique (UC) et colite indéterminée (IC) dans les 2 groupes. Groupe 1: malades âgés de plus de 60 ans. Groupe 2: malades âgés de moins de 60 ans.



**Fig. 2** - Annual incidence rate of CD and UC by age. Taux d'incidence annuelle de la maladie de Crohn (CD) et de la rectocolite hémorragique (UC) en fonction de l'âge.



**Tableau I.** - Incidence and main characteristics of Crohn's disease in patients > 60 years old and < 60 years old. Incidence et caractéristiques cliniques de la maladie de Crohn chez les malades > 60 ans et < 60 ans.

	> 60 years old	<60 years old	P
Proportion among all IBD patients (%)	23/60 (38)	114/210 (54)	0.04
Annual incidence per 100,000 inhabitants	3.45	4.8	0.18
Female/male	1.3	1.6	0.84
Mean age, years (range)	66.8 (60-84)	30.3 (15-54)	-
Median duration of symptoms before diagnosis, months (range)	7.5 (1-24)	6 (1-24)	0.17
Family history of IBD, % (n)	13 (3)	13.3 (15)	0.98
Location, % (n)			
• Small bowel	39.1 (9)	43.9 (50)	0.65
• Small and large bowel	43.5 (10)	33.3 (38)	0.37
• Large bowel	13.0 (3)	18.4 (21)	0.77
• Perineal disease	4.3 (1)	1.8 (2)	0.46
• Other sites	0 (0)	2.6 (3)	0.98

**Tableau II.** - Incidence and main characteristics of ulcerative colitis in patients > 60 years old and < 60 years old. Incidence et caractéristiques cliniques de la rectocolite hémorragique chez les malades > 60 ans et < 60 ans.

	> 60 years old	< 60 years	P
Proportion among all IBD patients	30/60 (50)	81/210 (39)	0.15
Annual incidence per 100,00 inhabitants	4.5	3.4	0.23
Female/male	0.7	0.49	0.55
Mean age, years (range)	68.6 (61-80)	34.3 (13-59)	-
Median duration of symptoms before diagnosis, months (range)	5 (1-24)	8.5 (1-24)	0.52
Family history of IBD, % (n)	0 (0)	9.76 (8)	0.11
Location, % (n)			
• Rectum	30.0 (9)	28.4 (23)	0.93
• Left colon	60.0 (18)	54.3 (44)	0.47
• Pancolitis	10.0 (3)	17.3 (14)	0.55

**Tableau III.** - Clinical manifestations of Crohn's disease in patients > 60 years old and in patients < 60 years old. Manifestations cliniques de la maladie de Crohn chez les malades > 60 ans et < 60 ans.

	> 60 years old	< 60 years old	P
Number of cases	23	114	
Fever, % (n)	13 (3)	24.6 (28)	0.35
Diarrhea, % (n)	60.9 (14)	85.1 (97)	0.014
Blood in feces, % (n)	26.1 (6)	22.8 (26)	0.75
Abdominal pain, % (n)	78.3 (18)	78.9 (90)	0.94
Weight loss, % (n)	30.4 (7)	53.5 (61)	0.04
Abdominal mass, % (n)	13.0 (3)	11.4 (13)	0.91
Intestinal obstruction, % (n)	17.4 (4)	7.9 (9)	0.3
Pseudo-appendicitis, % (n)	13 (3)	9.6 (11)	0.71
Extraintestinal symptoms, % (n)	4.3 (1)	22.8 (26)	0.045

**Tableau IV.** - Clinical manifestations of ulcerative colitis in patients > 60 years old and in patients < 60 years old. Manifestations cliniques de la rectocolite hémorragique chez les malades > 60 ans et < 60 ans.

	> 60 years old	< 60 years old	P
Number of cases	30	81	
Fever, % (n)	3.3 (1)	17.3 (14)	0.11
Diarrhea, % (n)	63.3 (19)	74.1 (60)	0.43
Bloody diarrhea, % (n)	63.3 (19)	61.7 (50)	0.67
Hematochezia, % (n)	6.7 (2)	6.2 (5)	0.99
Abdominal pain, % (n)	50 (15)	56.8 (46)	0.83
Weight loss, % (n)	33.3 (10)	21.0 (17)	0.14
Toxic megacolon, % (n)	0 (0)	2.5 (2)	0.99
Extraintestinal symptoms, % (n)	3.3 (1)	4.9 (4)	0.99

## Discussion

The global incidence of IBD was similar in the populations younger and older than 60 years (8.8/100,000 inhabitants/years vs 9/100,000 inhabitants/years). The annual incidence of UC in the older population tended to be higher than in the younger. The same results were observed in an European collaborative study on IBD [21]: the incidence rates remained constant or increased with age for men whereas those for women decreased. In our population of patients with CD, the annual incidence declined with age in both sex as shown in the European collaborative study [22]. On the contrary, data about CD collected over more than 50 years in the Cardiff area showed that the second peak in the eighth decade appeared as high as in the third decade [10].

As previously described in the general population of our area [9], CD was more frequent than UC. Such data were also observed in the Brussels area [18] and in northern France [16, 23], whereas UC is usually the most frequent IBD in the rest of Europe [22, 24, 25]. However, in the old population, the annual incidence tended to be higher for UC than for CD and the proportion of CD among the whole group of IBD was significantly lower in the elderly than in younger individuals. This fact was also observed in northern France [26] and in London [17].

Sex ratio was identical in the two groups of age; there were more women than men in the CD group and inversely in the UC group, as shown in most series in the literature [10, 16, 18, 20, 23, 24]. By contrast, in Puy-de-Dôme county of France [19], the female/male (F/M) ratio was 0.8 for CD and 1.1 for UC, whatever the age. In Brittany [25], the F/M ratio was 0.9 for CD except in the third decade (1.8) and 0.5 for UC. In a recent study conducted in the Netherlands [27], a F/M ratio of 0.75 has been observed in the older CD patients and the opposite in the young adults. By contrast, Carr and Schofield [28] reported a marked predominance of females (75%) in IBD patients over 60 years old.

The diagnosis delay was the same for people younger or older than 60 years. A difference has only been shown in a Dutch study: the time between onset of symptoms and definite diagnosis of CD was significantly shorter in the elderly patients [24, 26].

For CD, the various disease locations occurred with a similar frequency in both > 60 and < 60 populations in accordance with Dutch data [27]. In some studies a higher distal colonic location was observed in the old population [25, 29-32], while in another [33] more than half of the CD patients over 60 years had a small bowel involvement (terminal ileum).

In our study, the data for UC location are relatively uniform in both populations. Other previous studies [3, 26, 29] showed that left sided UC was more frequent in older patients and that colitis tended to be more extensive in younger ones. However, in a reference center at the university of Chicago [15], the proportion of pancolitis was higher in the elderly than in the younger patients (50 vs 20%, respectively).

Usually, clinical manifestations are much more diverse in Crohn's disease than in ulcerative colitis: abdominal pain sometimes associated with an abdominal mass, diarrhea, obstruction, anorectal diseases and systemic signs [1, 20]. In ulcerative colitis, bloody diarrhea is the cardinal symptom, even if some patients rather present with constipation [1, 20]. In this study, clinical manifestations were nearly the same whatever the age at onset of CD, apart from diarrhea, weight loss and extraintestinal symptoms; these manifestations were more frequent in the younger population. This might represent more aggressive disease in younger patients. This is similar to data from

the literature, apart from abdominal pain which seemed to be less frequent in people older than 60 years in other studies [23, 24, 34]. For UC, we did not find any significant difference between groups. Similar findings have been shown in previous studies [14, 15, 17].

Family history of IBD was as frequent in young as in old patients, by contrast with previous studies [24,32] showing that a positive family history was significantly more frequent in the young population. Authors of these studies concluded that disease with an early age at onset may represent a subgroup with a particularly strong genetic influence. However, our data are in accordance with a previous study carried out in the area of Liège [35] in which the age at diagnosis was the same in familial and sporadic CD.

In conclusion, our study shows a relatively high incidence of IBD in the elderly in the area of Liège. The incidence even tended to be higher in the elderly than in the young population for UC.

Among the epidemiological and clinical characteristics, there was no striking difference. This suggests that old age at onset may not represent a particular form of these diseases.

## REFERENCES

1. Podolsky DK. Inflammatory bowel disease (first of two parts). *N Engl J Med* 1991;325:928-37.
2. Satsangi J, Jewell DP, Rosenberg WM, Bell JI. Genetics of inflammatory bowel disease. *Gut* 1994;35:696-700.
3. Kirsner JB. Inflammatory bowel disease. Part I: Nature and pathogenesis. *Dis Mon* 1991;37:605-66.
4. Kirsner JB. Inflammatory bowel disease. Part I I: Clinical and therapeutic aspects. *Dis Mon* 1991;37:669-746.
5. Hugot JP, Chamaillard M, Zouali H, Lesage S, Cezard JP, Belaiche J, et al. Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease. *Nature* 2001;411:599-603.
6. Ogura Y, Bonen DK, Inohara N, Nicolae DL, Chen FF, Ramos R, et al. A frameshift mutation in NOD2 associated with susceptibility to Crohn's disease. *Nature* 2001;411:603-6.
7. Louis EJ, Collard A, Oger AF, De Groote E, Belaiche J. Location and behavior of Crohn's disease according to Vienna classification: evolution over the course of the disease (abstract). *Gastroenterology* 2001;120(S1):754.
8. Grimm IS, Friedman LS. Inflammatory bowel disease in the elderly. *Gastroenterol Clin North Am* 1990;19:361-89.
9. Latour P, Louis E, Belaiche J. Incidence of inflammatory bowel disease in the area of Liège: a three years prospective study (1993-1996). *Acta gastroenterol belg* 1998;61:410-3.
10. Rose JD, Roberts GM, Williams G, Mayberry JF, Rhodes J. Cardiff Crohn's disease jubilee: the incidence over 50 years. *Gut* 1988;29:346-51.
11. Eisen GM, Schutz SM, Washington MK, Burton CS, Sidhu-Malik N, Wilson JA. Atypical presentation of inflammatory bowel disease in the elderly. *Am J Gastroenterol* 1993;88:2098-101.
12. Akerkar GA, Peppercorn MA. Inflammatory bowel disease in the elderly. Practical treatment guidelines. *Drugs Aging* 1997;10:199-208.
13. Brandt LJ, Dickstein G. Inflammatory bowel disease: specific concerns in the elderly. *Geriatrics* 1989;44:107-11.
14. Fleisher DE, Grimm IS, Friedman LS. Inflammatory bowel disease in older patients. *Med Clin North Am* 1994;78:1303-19.
15. Lashner BA, Kirsner JB. Inflammatory bowel disease in older people. *Clin Geriatr Med* 1991;7:287-99.
16. Gower-Rousseau C, Salomez JL, Dupas JL, Marti R, Nuttens MC, Votte A, et al. Incidence of inflammatory bowel disease in Northern France (1988-1990). *Gut* 1994;35:1433-8.
17. Gupta S, Saverymuttu SH, Keshavarzian A, Hodgson HJ. Is the pattern of inflammatory bowel disease different in the elderly? *Age Ageing* 1985;14:366-70.
18. Van Gossum A, Adler M, De Reuch M, Devis G, Fiasse R, Vanheerwerzwin R, et al. Epidemiology of inflammatory bowel disease in Brussel's area (1992-1993). *Acta Gastroenterol Belg* 1996;59:7-9.
19. Nordenvall B, Brostrom O, Berglund M, Monsen U, Nordenstrom J, Sorstad J, et al. Incidence of ulcerative colitis in Stockholm County 1955-1979. *Scand J Gastroenterol* 1985;20:783-90.

20. Brandt LJ, Boley SJ, Milsudo S. Clinical characteristics and natural history of colitis in the elderly. *Am J Gastroenterol* 1982;77:382-6.
21. Flamenbaum M, Zenut M, Aublet-Cuvelier B, Larpent JL, Fabre P, et al. Incidence des maladies inflammatoires du tube digestif dans le département du Puy-de-Dôme en 1993 et 1994. *Gastroenterol Clin Biol* 1997;21:491-6.
22. Shivananda S, Lennard-Jones J, Logan R, Fear N, Price A, Carpenter L, et al. Incidence of inflammatory bowel diseases across Europe: is there a difference between north and south? Results of the European Collaborative Study on Inflammatory Bowel Diseases (EC-IBD). *Gut* 1996;39:690-7.
23. Gower-Rousseau C, Grandbastien B, Cortot A, Colombel JF. Epidemiology of inflammatory bowel diseases: is there a "Belgian-French exception"? *Acta Gastroenterol Belg* 1996;59:2.
24. Ekblom A, Helmick C, Zack M, Adami H. The epidemiology of inflammatory bowel diseases: a large population-based study in Sweden. *Gastroenterology* 1991;100:350-8.
25. Pagenault M, Tron I, Alexandre JL, Cruchant E, Dabadie A, Chaperon J, et al. Incidence des maladies inflammatoires du tube digestif en Bretagne (1994-1995). *Gastroenterol Clin Biol* 1997;21:483-90.
26. Gower-Rousseau C, Quinton JF, Nuttens MC, Desreumaux P, Colombel JF, Cortot A. Maladies inflammatoires chroniques de l'intestin (MICI) chez les sujets de plus de 60 ans: étude épidémiologique dans la région Nord Pas De Calais (1988-1990) (abstract). *Gastroenterol Clin Biol* 1994;18 (2bis):A13.
27. Wagtmans MJ, Verspaget HW, Lamers CB, van Hogezaand RA. Crohn's disease in the elderly: a comparison with young adults. *J Clin Gastroenterol* 1998;27:129-33.
28. Carr N, Schofield P. Inflammatory bowel disease in the older patient. *Br J Surg* 1982;69:223-5.
29. Softley A, Myren J, Clamp SE, Bouchier IA, Watkinson G, De Dombal FT. Inflammatory bowel disease in the elderly patient. *Scand J Gastroenterol Suppl* 1988;144:27-30.
30. Fabrieus PJ, Gyde SN, Shouler P, Keighley MR, Alexander-Williams J, Allan RN. Crohn's disease in the elderly. *Gut* 1985;26:461-5.
31. Feczko PJ, Barbour J, Halpert RD, Ackerman LV. Crohn's disease in the elderly. *Radiology* 1985;157:303-4.
32. Polito JM 2nd, Childs B, Mellits ED, Tokayer AZ, Harris ML, Bayless TM. Crohn's disease: influence of age at diagnosis on site and clinical type of disease. *Gastroenterology* 1996;111:580-6.
33. Shapiro PA, Peppercorn MA, Antoniolio DA, Joffe N, Goldman H. Crohn's disease in the elderly. *Am J Gastroenterol* 1981;76:132-7.
34. Harper PC, McAuliffe TL, Beeken WL. Crohn's disease in the elderly. A statistical comparison with younger patients matched for sex and duration of disease. *Arch Intern Med* 1986;146:753-5.
35. Franchimont D, Belaiche J, Louis E, Simon S, Grandbastien B, Gower-Rousseau C, et al. Familial Crohn's disease: a study of 18 families. *Acta gastroenterol belg* 1997;60:134-7.